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14. ABSTRACT This project is to perform translational research tasks needed to prepare an intracortical visual prosthesis (ICVP) for testing in a human. No human trial testing of the prosthesis will occur under the funded work. Preparatory tasks include final maturation of the implantable hardware, pre FDA IDE testing of the ICVP in non-human primates, reliability and biocompatibility testing, development of a human testing protocol, development of a human volunteer selection and assessment protocol, preparation of an investigation device exemption application (IDE) to the FDA. Progress to-date has been somewhat hampered by delayed approval of the psychology testing protocols (human subjects), and the animal testing protocols (non-human primates), by the USARMYMC. However, all protocol approvals have now been obtained. This delay has also slowed the spending of funds for these areas within the first year. The work focused on technology maturation has been highly productive. Sample stimulator units have been subjected to brutal environmental testing with 100% survival. Larger numbers of stimulator units are in the process of being constructed to provide statistical power for the environmental testing. Following the human protocol acceptances, work has commenced at both IIT and Johns Hopkins for the development of the testing and assessment protocols. A graduate student from IIT has initiated work within the laboratory of Dr. Dagnelie at JHU. Analysis of interview data from the earlier Dobelle visual prosthesis recipients has already yielded valuable insight about the volunteer recruitment and participation process. Sixteen publications and presentations have resulted from the funded work, and several publications are in preparation. While the project is projected for a 1-year no-cost extension request, due to the slow start-up, it is anticipated that by the end of the project all parts of the SOW will be complete, with the ICVP ready for clinical testing in a human trial.					
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INTRODUCTION

The objective of this project is to prepare for clinical feasibility testing of an intracortical visual prosthesis (ICVP) in humans. Our hypothesis is that an ICVP is technically and surgically feasible, has a sufficient likelihood of sensory benefit to warrant human testing, and that our ICVP team is at the point of readiness for proceeding towards a first human clinical trial. While the project will NOT support human testing, per se, it will accomplish all of the necessary steps to prepare the ICVP for testing in a human volunteer. The study uses a well-established project team lead by the Illinois Institute of Technology comprised of: Sigenics, Inc, MicroProbes for Life Science (MLS), University of Chicago (UC), Huntington Medical Research Institutes (HMRI), and Johns Hopkins University (JHU). The project work addresses a military-relevant health problem of compensating for vision loss because over 90% of those individuals with blindness, in the military and civilian population are not gainfully employed and often suffer from depression, social isolation, and a significantly-reduced quality of life.

This project has been granted a 1-year no-cost extension by TATRC. Owing to delays in obtaining human subject and animal subject approval from TATRC/USAMC (due in part to the unfamiliarity of IIT's Office of Sponsored Research with USAMC procedures) the human subject and animal work was delayed for approximately 1 year. Therefore, those portions of the project have lagged behind the other work.

THE STATEMENT OF WORK (SOW)

Our long-term hypothesis to be tested is that spatial-temporal electrical stimulation of the cortical visual system can provide usable visual sensation and restoration for those individuals with blindness. The objective of this proposed project is to make possible feasibility testing of an intracortical visual prosthesis (ICVP) in humans. While the proposed project will NOT support human testing, per se, it will accomplish all of the necessary steps to prepare the ICVP for testing in a human volunteer. The proposed work addresses a military-relevant health problem of compensating for vision loss because over 90% of those individuals with blindness, in the military and civilian population are not gainfully employed and often suffer from depression, social isolation, and a significantly-reduced quality of life. The potential contribution that the proposed study could make to addressing these issues is that by preparing the ICVP for clinical testing, a potentially ground-breaking alternative could become available to those with blindness.

For the past decade, Illinois Institute of Technology (IIT) has lead a team-based project, consisting of multiple institutions, to advance the ICVP - for which micro-sized wire electrodes provide electrical stimulation directly to the visual cortex. During this time, accomplishments have been achieved for development of electrode materials, electrode array fabrication, implantable wireless hardware design, implantable stimulator fabrication and stress testing, non-human primate psychophysics, normal human psychophysics, surgical feasibility assessment, and psychological assessment of potential and past vision prosthesis recipients. Our hypothesis is that an ICVP is technically and surgically feasible, has a sufficient likelihood of sensory benefit to warrant human testing, and that our ICVP team is at the point of readiness for proceeding towards a first human clinical trial.

The proposed study will use a well-established project team lead by Dr. Troyk of IIT. This team is comprised of six institutions: Illinois Institute of Technology, Sigenics, Inc, MicroProbes for Life Science (MLS), University of Chicago (UC), Huntington Medical Research Institutes (HMRI), and Johns Hopkins University (JHU). Each member of the team brings highly-targeted expertise to address the following six program components. In order to accomplish the ambitious long-term project goal, key steps must be taken to prepare our ICVP system for clinical testing. These comprise the SOW and are (the order of organizations indicates task responsibility):

1. Design evaluation and fabrication of large numbers of implantable electrode array/stimulator modules (ICVP modules) under GLP and GMP conditions with suitable documentation for satisfying regulatory submission needs, within sustainable commercial organizations. (Y1 – IIT, MLS, Sigenics)
2. Testing of, and prediction of long-term biocompatibility and survivability for, (ICVP modules) in animal and laboratory evaluations. (Y1/Y2 – IIT, UC, HMRI, Tox Monitor Labs)

3. Design and testing of a real-time psychophysical assessment and testing system for evaluation of an ICVP recipient, and design and fabrication of a first-generation portable image processing system for converting electronic images into cortical stimulation neural coding patterns (Y1/Y2 – JHU, IIT, Sigenics)
4. Design and implementation of a volunteer recruitment and evaluation process that preserves subject protection, integrity, and maximizes project scientific significance. (Y1/Y2 – IIT, UC)
5. Constitute a team structure within a clinical setting for preparation of surgical implantation and human subject care. Y1/Y2 – UC, IIT)
6. Preparation and submission of an FDA IDE application for a human trial. (Y2 – IIT, UC, JHU)

PROGRESS FOR SOW TASK 1

TASK 1. Design evaluation and fabrication of large numbers of implantable electrode array/stimulator modules (ICVP modules) under GLP and GMP conditions with suitable documentation for satisfying regulatory submission needs, within sustainable commercial organizations.

The IVCP hardware system is comprised of two key components: the implantable stimulator modules (ISM), and the extracorporeal telemetry controller (TC). Both of these have undergone extensive maturation during the second-year project period.

The ISM is comprised of an application-specific-integrated circuit (ASIC), placed within an electrode array that contains a ceramic substrate which maintains the position of the electrodes while serving as an interconnection means between the ASIC and the electrodes, as shown in Figure 1. The electrodes are fabricated from pure iridium, and Activated Iridium Oxide Film (AIROF) is electrochemically grown on the electrode after all of the encapsulation processes have been completed. The AIROF film dramatically enhances the injectable charge capacity of the electrodes, and the growth of the film following the encapsulation processes is necessary because of the high curing temperatures for the silicone encapsulant (150C). The AIROF film cannot tolerate the elevated temperature without resulting in destruction. Therefore a unique functionality of the ASIC is that it can be commanded over ISM wireless link to activate the electrodes after the assembly has been fully encapsulated.

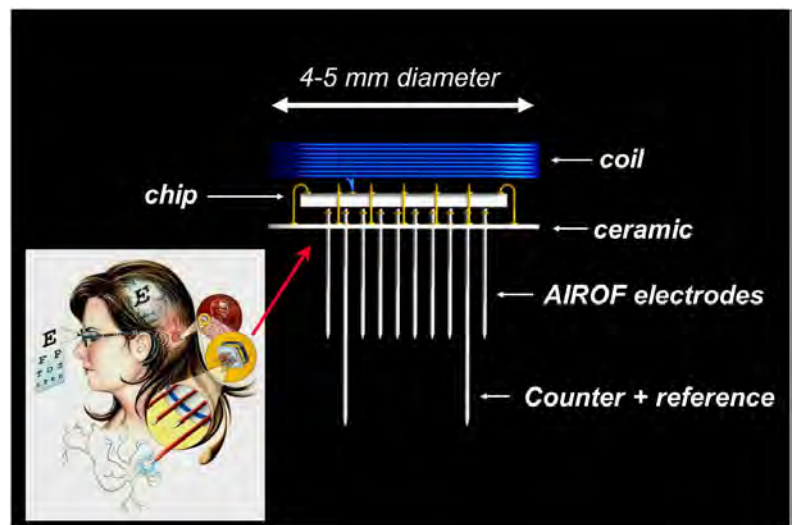


Figure 1 – Illustration of the ISM showing the internal components

During this past project year, the assembly process for the ISM has been matured and demonstrated by the fabrication of several ISMs. Some of these units have been tested in accelerated laboratory tests, as described in Progress for SOW TASK 2, below. The complete assembly process is shown in Figures 2 and 3. At the subassembly level, the ceramic substrate is populated with electrodes. Then the ASIC is attached to the substrate with subsequent wirebonding. The coil is directly wirebonded to the ASIC, and the ISM is encapsulated in a mold, to produce the ISM assembly shown in Figure 4. Variations upon the ISM, in which the coil is fully integrated with the electrodes and ASIC are shown in Figure 5, in which a pigtail coil is attached to the ASIC using a 2-wire cable. This pigtail ISM assembly allows for an extended range of magnetic operation, albeit with the addition of the tethering 2-wire cable.

Stimulator Assembly

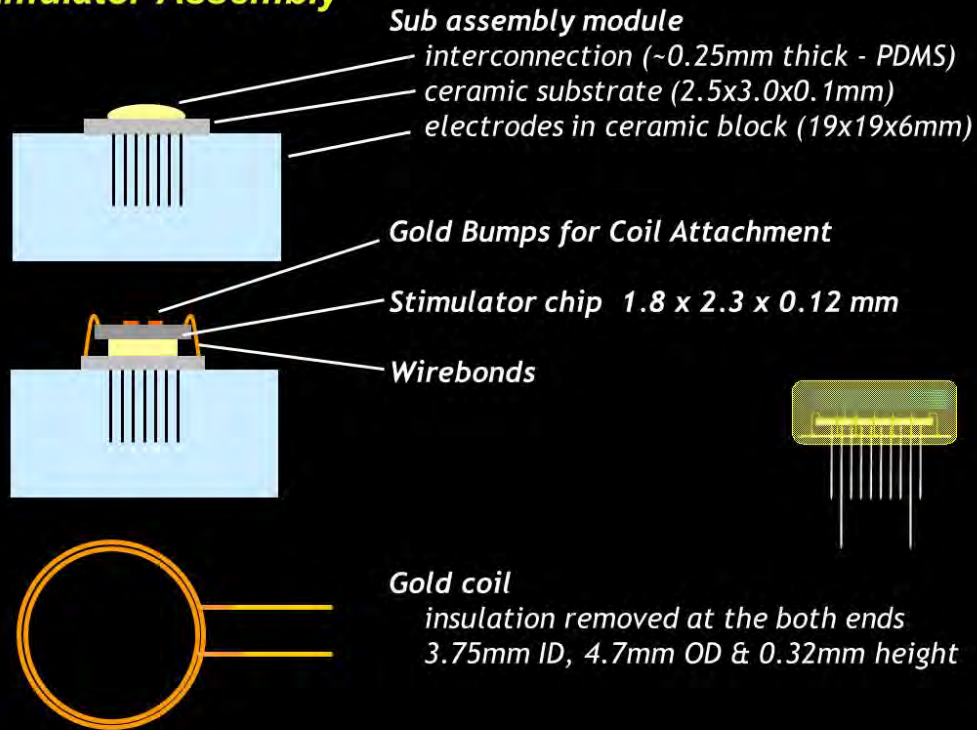


Figure 2 – Preliminary ISM assembly steps

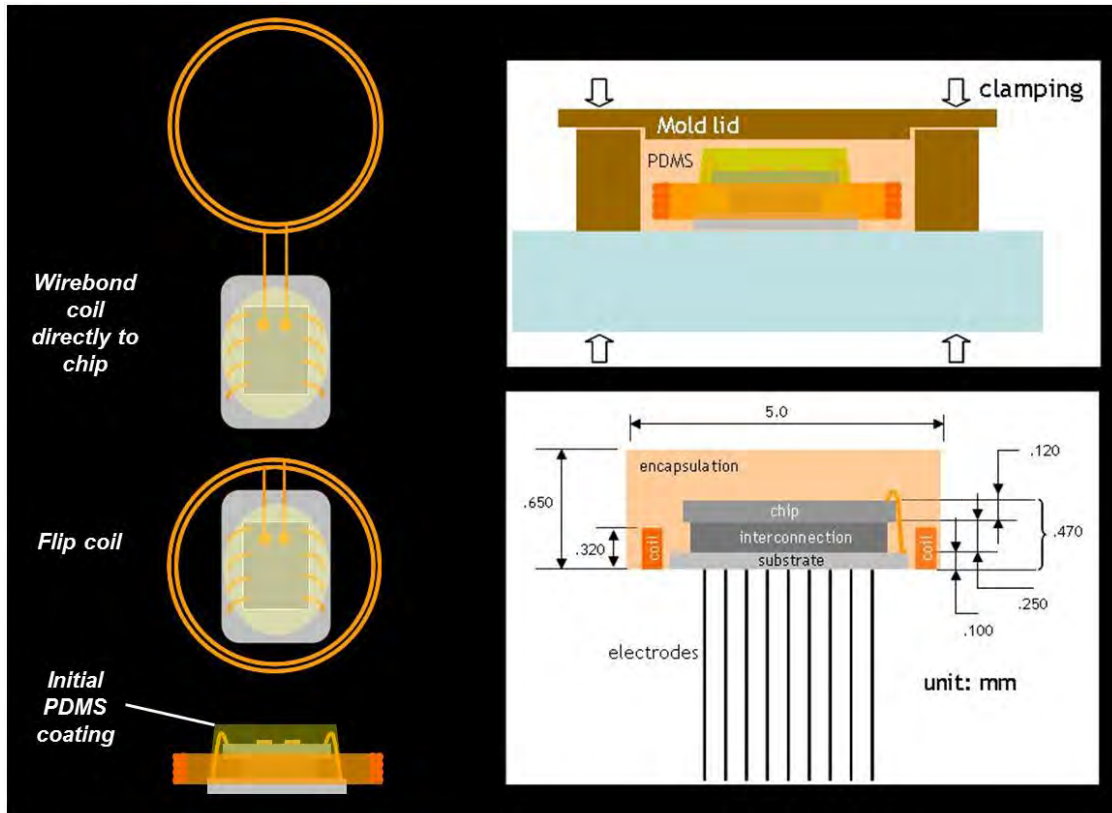


Figure 3 – Final ISM assembly steps

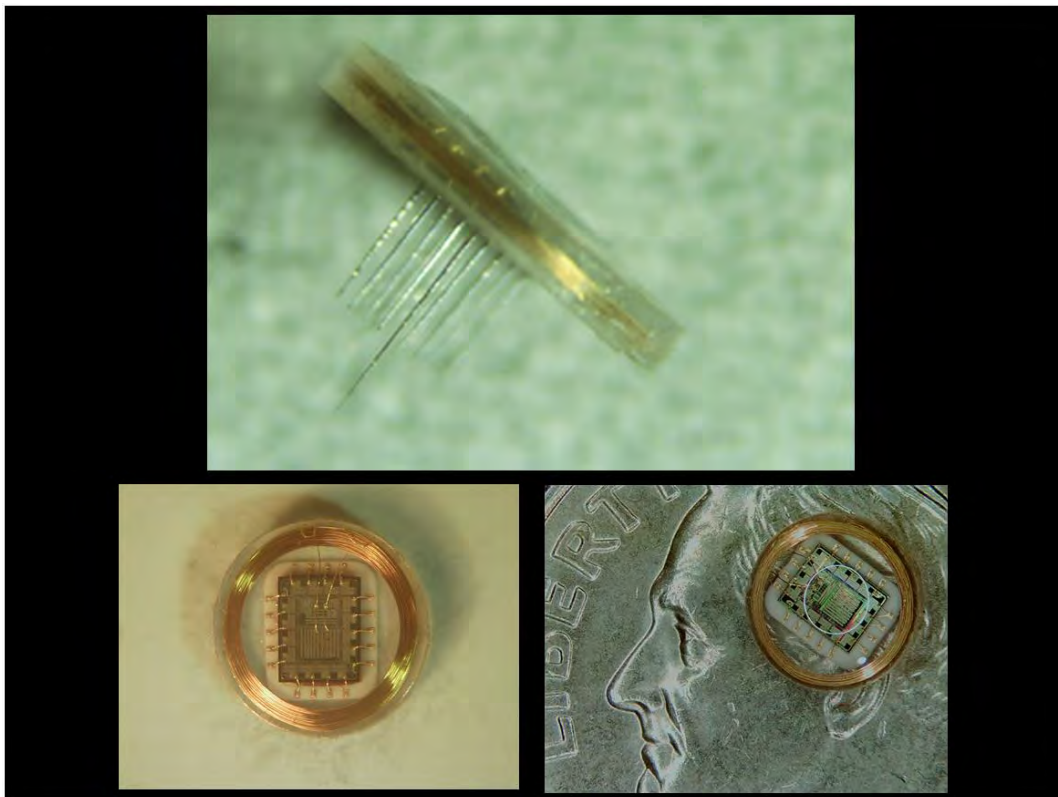


Figure 4 – Fully assembled ISM device

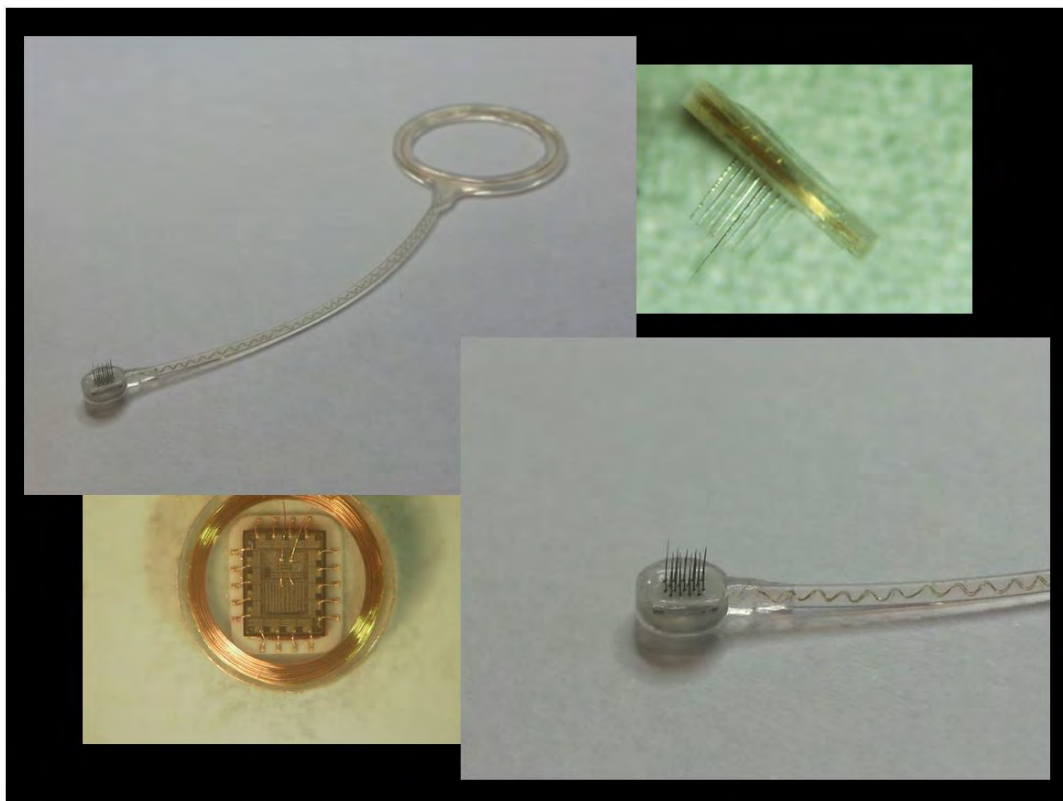
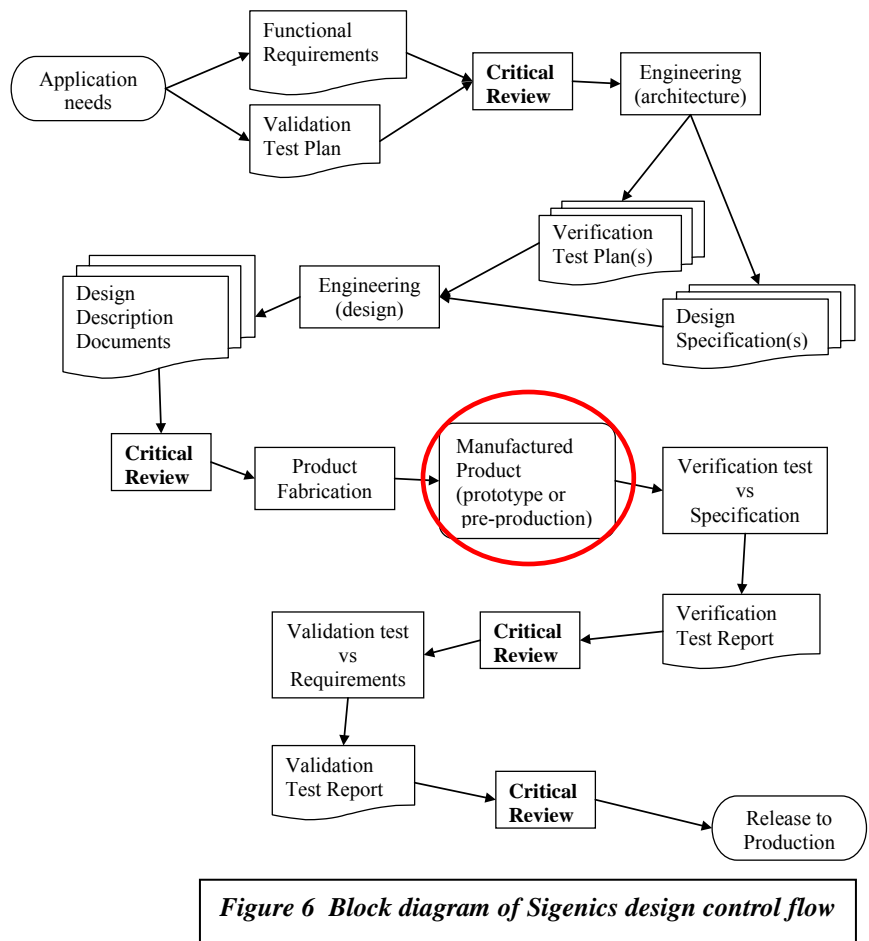


Figure 5 – Differing ISM models showing leaded vs non-leaded designs

The ASIC is being reviewed using a controlled procedure for formal review of ASICs within Sigenics. This is the same process that is used for commercial, and military-grade, ASICs that are manufactured by Sigenics. This process is shown in Figure 6, below, as presented in the project proposal.

Owing to the fact that the ASIC design pre-existed the start of the design control flow process, design review has not followed a linear pathway. Currently the review process is at the pre-production step as shown in Figure 6. The circuit design has been found to be sound, and absent critical flaws. Certain performance limitations have been identified, and are consistent with the decisions made at the time of initial design process, dating back to 2004. An assessment was made as to whether the ASIC design would notably benefit from revising the circuitry and fabricating within a smaller geometry process: 0.35 micron, rather than the current 0.8 micron technology. Over 75% of the ASIC circuitry is digital in nature. Unquestionably the physical size of this digital circuitry would shrink to approximately 1/3 – 1/4 the current size. Yet the real question to be considered is whether there would be a performance or reliability advantage to the geometry reduction. The current assessment is that no performance advantage would be achieved. The current ASIC design has the advantage of historical testing and use over the past five years. Therefore, the assessment result has been to retain the current design. Formal design review, specification, and acceptance test procedure documents have been completed. CX08 wafers will be fabricated in Y3 that contain the approved ISM ASIC design. In this manner, the necessary traceability and hardware procurement control is being implemented, as needed to support the IDE application.



The telemetry controller (TC) component, used for extracorporeal powering and control of the ICVP stimulator modules, has undergone design maturation within Sigenics. The TC reverse telemetry system, used to wireless monitor the critical system operational parameters (power supply, electrode polarization potentials), was completely redesigned in Y2.

This past year saw the demonstration of the first time that all sixteen iridium electrodes were simultaneously activated over the wireless inductive link. Using three completed ISM assemblies and a standard TC component, all of the ISM iridium electrodes were activated via wireless command telemetry.

Fabrication processes for the ISM have been further refined at IIT, in cooperation with MicroProbes for Life Sciences (MLS), towards the goal of transferring the entire manufacturing process to MLS. This is necessary to implement the upscale of the manufacturing of the ISM units in larger numbers.

In summary, progress made for SOW Task 1 now allows for fabrication of a large number of modules to be accomplished at IIT and MLS, with transfer exclusively to MLS for the production of ISM units to be used in toxicology testing, environmental stress testing, and animal implantations. In-vivo implantations are planned for Y3.

PROGRESS FOR SOW TASK 2

Task 2. Testing of, and prediction of long-term biocompatibility and survivability for, (ICVP modules) in animal and laboratory evaluations

Although approval of the animal protocol was accomplished in January of 2014, Y2 did not see the implantation of ISM units in primate experiments. These are planned for Y3.

Rather, the focus of the ICVP modules (called ISMs) has been approached within accelerated stress testing in an unprecedented manner. Here, we present those results using text as presented in a recent IEEE EMBC publication:

Various examples of environmental testing for commercial IC devices and passive components can be referred to for assessing the reliability of implantable devices. One of the investigations for the physical and electrical degradation of plastic encapsulated power transistor demonstrated that following environmental tests, (temperature cycling, HAST, THB) delamination failures were seen between the molding compound and die/lead frame, as well as elevated electrical leakage currents. Such degradation was considered to be critical because it might cause bond wire breakage and facilitate moisture penetration on to the die resulting in contamination and possible corrosion in a

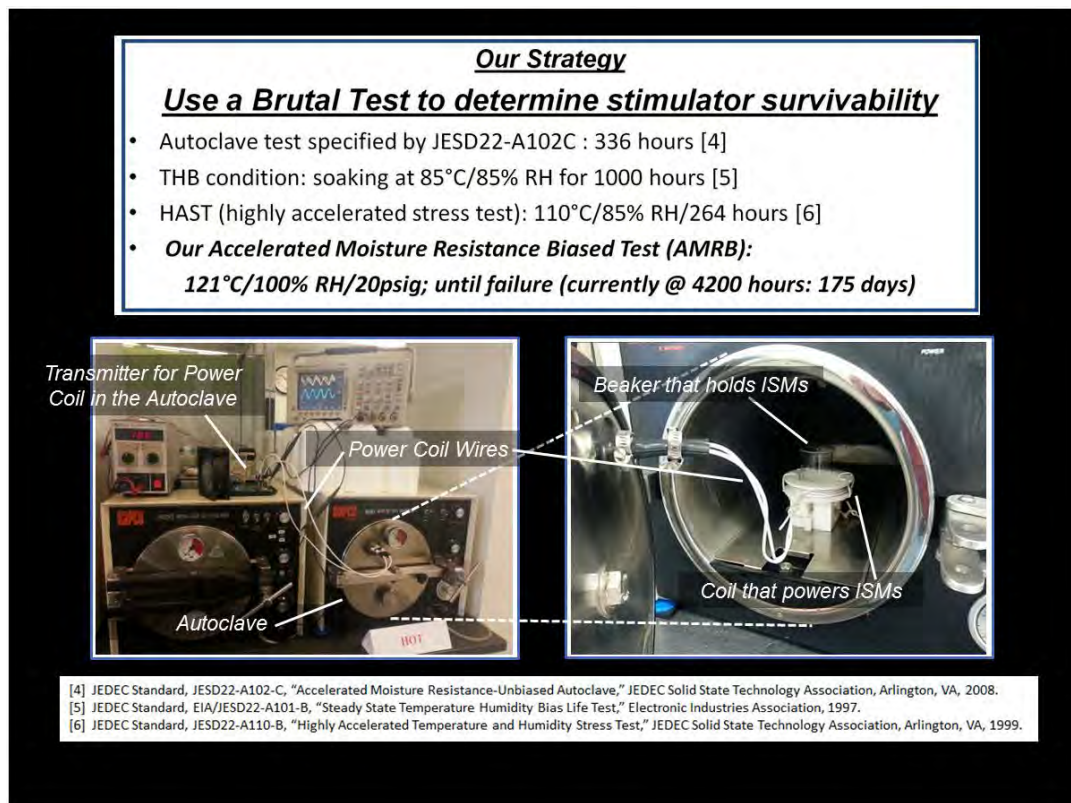


Figure 7 – Test setup for ISM accelerated testing

For the reliability evaluation of the ICVP device, we selected an accelerated moisture resistance-biased autoclave test. Similar to temperature-humidity-bias (THB), failures during the autoclave test (normally conducted at 121°C and 100% relative humidity) with the devices in storage, and under electrical bias, are typically caused by moisture-induced swelling of encapsulation polymer, leakage currents, and corrosion of metallization.

As shown in Figure 7, for the autoclave test with bias, a power transmission coil with an inductance of 8.4uH was fabricated using AWG14 stranded copper wire insulated with thin Teflon. The wire was wound using a Teflon bobbin of 3 inches in diameter to form a power coil that was driven by a 5 MHz Class E converter.

The magnitude of wireless power transmission and actual current inside the power coil, was monitored to ensure correct powering of the ASICs. Every 24 hours, the four devices were taken out for visual inspection and the reverse telemetry test. The power coil assembly was inspected whenever reduced current was seen in the power coil. The harsh autoclave environment proved highly damaging to the 5MHz power coil, significantly more than the devices under test. It was challenging to maintain proper Class-E tuning under the conditions of water infiltration into the power coil. In some cases it was necessary to pause the test while the power coil assembly was dried in an oven for couple of hours or replaced with a new coil.

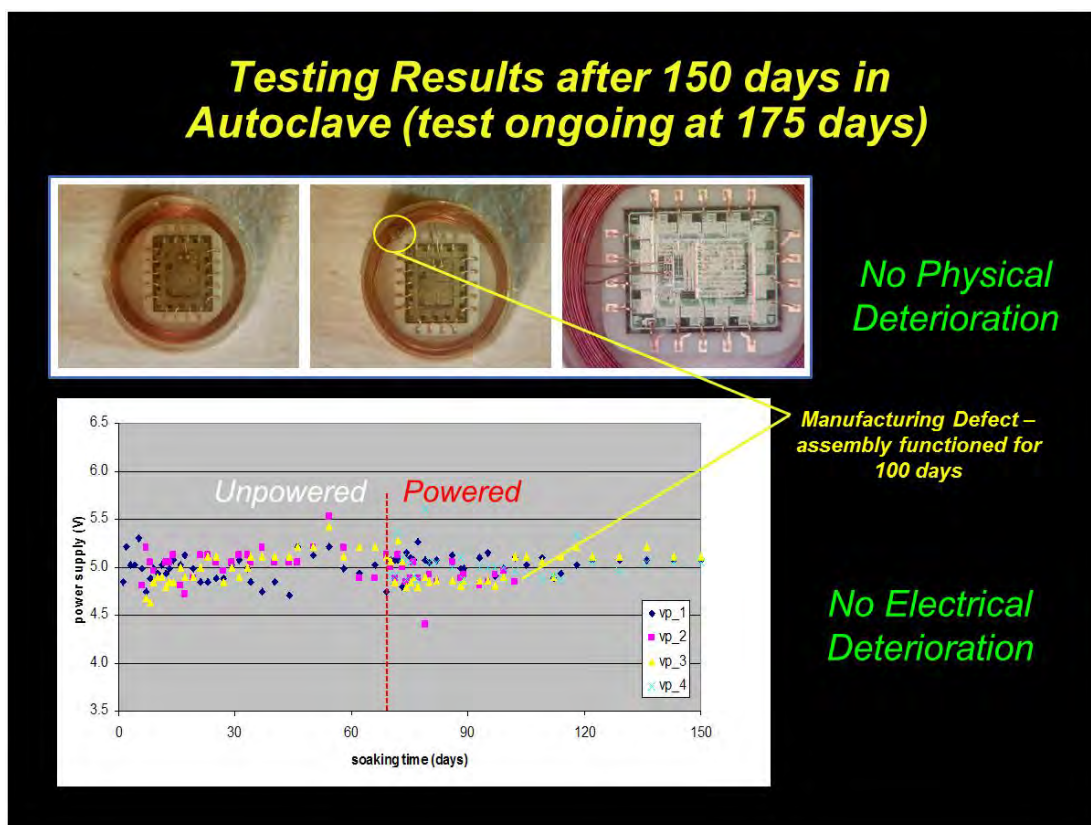


Figure 8 – Test results from Autoclave-based accelerated testing

Three devices were initially soaked, without being powered, in the chamber to determine if any electrical degradation or physical deterioration would occur due to physical stress alone. Following each 24 hours of soaking, the devices were taken out of the chamber for the reverse telemetry test and visual inspection under the light microscope. Later, the test interval was increased to every two days, and then to four days, based on the previous test results. After 1600 hours of soaking without bias, and no indication of physical or electrical deterioration, an additional accelerated moisture resistance test under wireless powering, was performed on these three pre-stressed devices. For comparison, a new stimulator device package, not previously stressed under storage alone, was added to the autoclave testing with bias.

Measurements of the ASIC internal power supply, by the reverse telemetry, of the devices tested without and with power transmission for 150 days are summarized in Figure 8. The data from each device were normalized based on the stimulator ASIC power supply voltage of 5Volts.

Figure 8 shows the bias (power supply) voltage data measured from each device under test. In practice, the data are transmitted by modulating the width of the reverse telemetry carrier envelope, with the duration of transmission encoding the voltage value. In the telemetry control board, an FPGA decodes the carrier pulse duration into the bias voltage. The variation in bias voltage from each device measured less than 1 volt over 150 days of testing without any specific trend. The scatter in the data of Figure 4 is substantially due to the variation in the position of the device with respect to the power/receiver coils causing expected power supply variations, subtle reverse telemetry shifts, and decoding jitter. The variation is not representative of deterioration of the devices. To the contrary, the very fact that the reverse telemetry was maintained over the duration of the stress test is, alone, verification of the lack of device deterioration, since sensitive ASIC circuitry would undoubtedly cause cessation of reverse telemetry operation.

The Autoclave test specified by JESD22-A102C describes a maximum duration of 336 hours. THB condition shows a longer soaking at 85°C/85% RH for 1000 hours. Similarly, HAST (highly accelerated stress test) specifies tests at 110°C and 85% RH for 264 hours. The Accelerated moisture resistance test-biased used in this study was conducted under even more harsh environment of 121°C, 100% RH and 20psig for 3600 hours (and the test is currently on-going). As shown in Figure 8, defect-free devices are electrically functioning without any observable degradation, implying physical and electrical robustness of the ISM device.

Undoubtedly the question of what acceleration factor this test represents will be part of our upcoming discussions with the FDA. Unfortunately, from the standpoint of determining an acceleration rate, we have seen no failures. Acceleration rates are typically determined by calculating an activation energy, resulting from measurement of failure at two different temperatures. The lack of failures in our testing does not allow for the activation energy computation. Another method commonly used is to estimate that chemical reactions double for each 10 degrees C elevation above the service temperature. Considering that the service temperature of the ISM is 37 degrees C, then at a stress-test temperature of 121 degrees C (84 degree C rise above service), an acceleration factor of 337 would result. This means that for an accelerated test survival time of 175 days, that the predicted service lifetime would be at least 58,975 days, or 161 years. While our confidence in the prediction of this extreme lifetime is low, it does demonstrate the extremely brutal nature of this testing. In contrast, some earlier pacemaker testing allowed for boiling in saline for 2 weeks. Note that the acceleration factor calculation for our test does not take into account the increased pressure of 20psi, which would be expected to accelerate the water-induced failure reactions even more than the 337x factor.

In summary, our testing of the ISM devices over this past year have dramatically raised our confidence in the ISM packaging method, and our expectation for implanted lifetimes that will most likely exceed the practical length of a first clinical trial. Our continued testing for the Y3 will increase the “n” sample size and add the presence of saline fluid within the beaker of the autoclave – although the it is the presence of the water, and not the saline, which will drive the water-induced failure mechanisms of the ISM.

Following fabrication of a larger number of ICVP modules, we will commence toxicology testing, followed by animal testing in non-human primates.

PROGRESS FOR SOW TASK 3

Task 3. Design and testing of a real-time psychophysical assessment and testing system for evaluation of an ICVP recipient, and design and fabrication of a first-generation portable image processing system for converting electronic images into cortical stimulation neural coding patterns.

For this task, work has progressed at IIT, in combination with JHU. Under supervision of subcontract PI Gislin Dagnelie, PhD, Sr. Systems Manager Liancheng Yang and IIT graduate student Gayatri Kaskhedikar have developed phosphene mapping procedures allowing efficient and accurate creation of the spatial representation of each electrode’s phosphene in visual space, and conversely of spatial coordinates onto the implanted electrodes.

In accordance with the Statement of Work for this subaward, most of the effort in the past year has been devoted to improving mapping methods and phosphene simulations, in preparation for use of these methods in future blind implantees. The development of phosphene dynamic range procedures and phosphene-based image transformation

also received considerable attention, and software procedures for all 3 aspects of the project were developed in preparation for simulation tests in sighted subjects, carried out under separate funding (r01 EY021220, PI: Gislin Dagnelie, Ph.D.). Graduate student Gayatri Kaskhedikar spent several extended periods of time in the laboratory of her JHU advisor, Gislin Dagnelie, PhD, where in addition to her advisor she received assistance by Sr. Systems Manager Liancheng Yang and JHU undergraduate student Thomas Boucher.

In Ms. Kaskhedikar's study, the proposed methods for phosphene mapping in cortical prosthesis recipients will be developed initially by providing sighted individuals with simulated phosphenes. The functional adequacy of the map will be ascertained from the subject's ability to perform visually-guided tasks when provided with the simulated prosthetic vision obtained by the overlaying the phosphene map on the visual imagery.

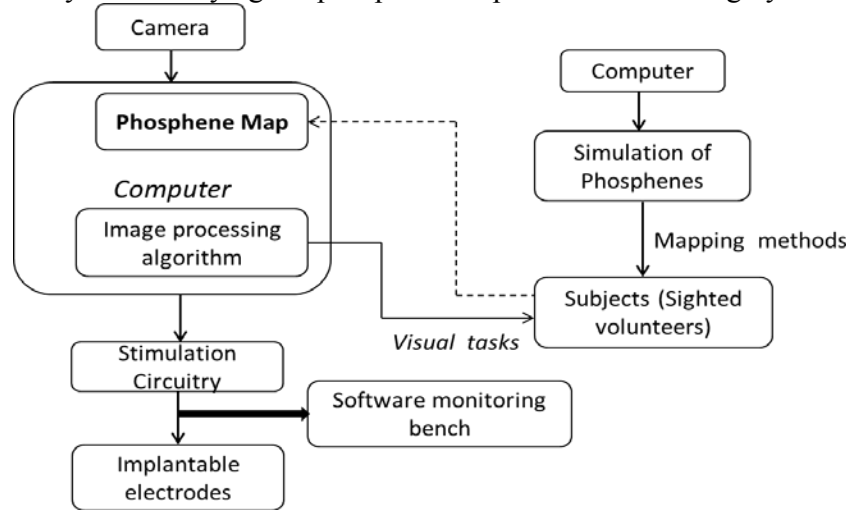


Figure 9. Design of the proposed experiments.

Ms. Kaskhedikar and Mr. Boucher worked out the calibration procedures for the laboratory data collection system consisting of: 1) a high-resolution display used to present simulated phosphenes to sighted individuals; 2) an infrared pupil tracking system capable of recording eye movements at 60 frames/s; and 3) a touchscreen allowing the viewer to indicate the perceived location of presented phosphenes. Three separate mapping methods were designed, implemented, and validated:

- A touchscreen-based absolute mapping method, in which the subject moves the finger across the touchscreen from the center to the perceived location of a phosphene, without breaking fixation from a central window verified by the eyetracker
- An eye movement method, in which the subject makes a saccadic eye movement to the remembered location of a briefly presented phosphene
- A relative mapping method, in which two phosphenes are presented in sequence, and the subject traces a line on the touchscreen representing the perceived direction of the 2nd phosphene relative to the 1st one.

Ms. Kaskhedikar worked out an analytical approach to combining the phosphene location information obtained from these 3 methods, taking into account the relative variability of each.

In addition to the considerable progress made in the area of phosphene mapping we have devised a rapid thresholding and dynamic range verification method, as well as an image transformation method for the presentation of common objects and space layout imagery through a phosphene “mask” obtained with the mapping methods described above. In the coming year, we will design quality metrics for the recognition of phosphene-based object recognition and wayfinding using these images. These metrics will be evaluated in sighted subjects, to gain confidence that they will be equally useful in blind cortical prosthesis recipients.

When Ms. Kaskhedikar is not at JHU, she is developing a portable image processing system that an implanted volunteer can take home during the clinical trial. Her present efforts, as part of her doctoral thesis, focus upon the development of an end-to-end ICVP diagnostic testing system, to assure that the proper commands will indeed be communicated to a family of ISM implanted devices.

In summary, the development of a testing system for mapping and evaluation of an implanted volunteer is of crucial importance to a future clinical trial. Similarly, availability of a portable system that the volunteer can take home, out of the laboratory, is, beyond doubt, one of the most important requirements for volunteers (as determined by our work on Task 4). Both of these essential system components have shown good progress during the past year.

PROGRESS FOR SOW TASK 4

4. Design and implementation of a volunteer recruitment and evaluation process that preserves subject protection, integrity, and maximizes project scientific significance.

With the USAMC IRB approval in place, during 2014, progress for Task 4 is proceeding rapidly.

Task 4 Start-up: The project start-up has consisted of the development of: a recruitment plan, an informed consent document, the research protocol, conducting of interviews of recipients of the Dobelle implant, preparation for focus group interviews, and analysis of data. The specifics of each activity are described below.

Understanding the psychological needs of potential volunteers is crucial to a successful clinical trial. Unless the volunteer is an authentic member of the research team, the likelihood of maximizing knowledge obtained from the trial is substantially reduced. Integration of the psychology component with the technical and medical components of our team is substantial. Students in Dr. Troyk's lab, who are pursuing the technology development, communicate regularly with students from Dr. Lane's lab who are involved with the development of the volunteer selection and evaluation protocols.

During the past year, the psychology team completed the individual interviews of the Dobelle recipients. The research team traveled to the recipients' homes, had the interviews transcribed and engaged in in-depth analysis of the data.

A systematic analysis of the transcribed data was conducted. The videotape and audiotape files of the fourteen participants were professionally transcribed verbatim and a digital file was created. After the transcriptions were complete a second person checked the translations and made minor suggestions to improve their accuracy. We reviewed the transcripts for accuracy, which established the official record for analysis. The two co-investigators and research assistant independently reviewed the transcripts and "open-coded" the narrative. We compared the results and reached agreement on a coding scheme to be used for axial coding. The narrative was then re-analyzed and coded so that each portion of the text was coded on at least one axis.

Once axial coding was completed, we reviewed each theme to determine whether it was justified or could be captured under a different theme. After the axes were agreed upon, we met with the principal investigator of the research team who reviewed the data and assisted in the organization and interpretation of the results. This process was used to develop broader themes; a hierarchical structure emerged from the themes that were agreed upon by all investigators.

The final analysis was presented at The Eye and the Chip in Detroit, Michigan, in September 2014 and also in a poster presentation at the Neural Interfaces Conference in Dallas, TX in June 2014. We are currently working on the first draft of the final manuscript of the Dobelle recipients for submission to the Journal of Neural Engineering.

The psychology team also recruited, screened and conducted three focus groups with individuals who are blind at the Chicago Lighthouse for the Blind. A total of 18 individuals participated in one of three focus groups over a period of two months. The focus groups lasted for two hours each and were audio and videotaped. The audio and video files have been transcribed. The final focus group with an additional 6 participants will be conducted in the upcoming year.

The psychology team has also been conducting in-depth research on the prior recruitment and screening protocols, as used in the Dobelle study. The co-investigator of the psychology team contacted Dr. Beth Seelig, psychiatrist who

screened the participants for an earlier version of the Dobelle implant. The plan is to utilize the information learned from the analysis of the Dobelle implant recipients and the focus groups conducted at the Chicago lighthouse to screen for problematic areas by way of a trained mental health practitioner.

In summary, the results from the Dobelle subjects interviews, and Chicago Lighthouse focus groups, are setting the foundation for the development of a volunteer selection and participation support protocol which will be developed in Y3.

PROGRESS FOR SOW TASK 5

Task 5. Constitute a team structure within a clinical setting for preparation of surgical implantation and human subject care.

The progress for this task has been excellent, and substantially unchanged from last year when the team structure was matured. Following changes in medical personnel at the University of Chicago, a highly qualified surgical and medical group is fully integrated with the technical personnel at IIT, MLS, and Sigenics. Involvement of HMRI has lagged somewhat owing to the delays in the non-human primate animal testing. However, we expect HMRI to be re-integrated into our team structure during Year 3.

The current project team includes:

The ICVP Team

IIT Colleagues:

Philip Troyk, Ph.D. – PI, bioengineer
Frank Lane, Ph.D. – psychologist
Margaret Huyck, Ph.D. – psychologist
Sungjae Suh, Ph.D. – material scientist
Gayatri Kaskhedikar – bioengineer
Sam Bredeson – bioengineer
Michael Davis, Ph.D. – ethicist

U of C Colleagues:

Sozari Chkhenkeli, MD - neurosurgeon
Jack Cowan, Ph.D. - mathematician
David Frim, MD - chief neurosurgeon
Royce Lee, MD - psychiatrist
Ben Roitberg, MD - neurosurgeon
Leo Towle, Ph.D. - neurophysiologist
Wim VanDrongelen, Ph.D. – neurophysiologist
Craig Wardrip, DVM – veterinarian

Other team members:

Marty Bak – (MicroProbes for Life Sciences) bioengineer
Stuart Cogan, DSc – (University of Texas, Dallas) bioengineer, material scientist
Gislin Dagnelie, Ph.D. – (Johns Hopkins University) psychophysicist
Conrad Kufka, MD – (NIH - retired) neurosurgeon
Doug McCreery, Ph.D. – (Huntington Medical Research Institutes) bioengineer, neuroanatomist
Ed Schmidt, Ph.D. – (NIH -retired) bioengineer

This team has all of the expertise needed for deployment of the ICVP in a clinical trial. The working relationships are intimate, with publications and conference presentations crossing disciplines.

In summary, progress on Task 5 has been substantial, with the assemblage of an unprecedented team of expert individuals who have working relationships that are active and unified towards the goal of the clinical trial.

PROGRESS FOR SOW TASK 6

Task 6. Preparation and submission of an FDA IDE application for a human trial.

This is the culminating Task for the project work. Preparatory work for accomplishing this task has been performed in the first two project years and includes: documentation of the technological status of the implantable hardware, development of a solid medical assessment for safety within a clinical trial, establishment of volunteer recruitment criteria, and an unprecedented understanding of potential volunteer needs, will form a solid ethical basis for presentation to the FDA, and a multi-parametric design of the first clinical trial experimental protocol. Prior to the end of 2014, we will schedule a preliminary visit with the FDA. Informal discussions with the relevant FDA officials has already occurred during the attendance of our team at the 2014 Eye and the Chip, international congress on vision prostheses.

During Year 3, we will engage the services of a consultant to advise us on the mechanics of IDE preparation. We plan to submit the IDE application under the “early feasibility program” at the FDA. In this program, the assumption is that the device being tested is not in final form. This project will benefit from the emerging recognition that proof-of-concept approaches to device testing are appropriate, provided that safety can be reasonably assured. The preliminary visit to the FDA in Year 2 will establish the appropriateness of our project plan and form the basis for the IDE application preparation.

In summary, the combination of the past two year’s efforts for Tasks 1-5 have formed a solid basis for the pursuit of the IDE goal for Task 6 in the second project year.

KEY RESEARCH ACCOMPLISHMENTS

- Demonstration of the robustness and reliability of the ICVP technology, as shown in accelerated laboratory testing, resulting in a reliable implantable system ready for clinical deployment
- Testing of novel and advanced psychophysical testing methods
- Implementation of a portable ICVP image processing system
- Establishment of psychological testing and volunteer selection protocols based upon experiences of prior visual prosthesis recipients and focus groups of potential volunteers.
- Formation of a multi-disciplinary ICVP team, with on-going and active participation by all team members.
- Foundation for submission of IDE to the FDA for an ICVP clinical trial.

REPORTABLE OUTCOMES

Presentations during the post-award notification/pre-award start date period

1. Frank John Lane, Kristian Nitsch, Margaret Huyck, Philip Troyk, Ken Schug, "Perspectives of optic nerve prostheses," *Disability and Rehabilitation: Assistive Technology* : 1–9. (doi:10.3109/17483107.2014.961178) Posted online on 26 Nov 2014.
2. Sungjae Suh; Troyk, P.R.; Zhe Hu, "Accelerated-stress reliability evaluation for an encapsulated wireless cortical stimulator," *Engineering in Medicine and Biology Society (EMBC), 2014 36th Annual International Conference of the IEEE* , vol., no., pp.442,445, 26-30 Aug. 2014
3. Bredeson, S.D.; Troyk, P.R., "Device for the implantation of neural electrode arrays," *Engineering in Medicine and Biology Society (EMBC), 2014 36th Annual International Conference of the IEEE* , vol., no., pp.434,437, 26-30 Aug. 2014
4. Samuel D. Bredeson, Philip R. Troyk, Sungjae Suh, and M. Bak, "Investigation of Long-Term Electrical Degradation in Neural Recording and Stimulation Microelectrode Arrays," 6th Annual International IEEE EMBS Conference on Neural Engineering San Diego, California, 6 - 8 November, 2013 pp. 621 -624
5. Gayatri P. Kaskhedikar, Zhe Hu, Gislin Dagnelie and Philip R.Troyk, "Proposed Intracortical Vision Prosthesis System for Phosphene Mapping and Psychophysical Studies," 6th Annual International IEEE EMBS Conference on Neural Engineering San Diego, California, 6 - 8 November, 2013 pp. 880-882
6. Z. Hu, P. Troyk, G. DeMichele, D. Kerns, M. Bak, "A laboratory instrument for characterizing multiple microelectrodes," 35th Annual International Conference of the IEEE EMBS pp. 1558 – 1561, 2013
7. S. Bredeson, P. Troyk, S Suh, M. Bak. "Identification and Quantification of Electrical Leakage Pathways in Floating Microelectrode Arrays." 35th Annual International Conference of the IEEE EMBS pp. 1542 – 1545 2013
8. Troyk, P.; Hu, Z., "Simplified Design Equations for Class-E Neural Prosthesis Transmitters," *IEEE Transactions on Biomedical Engineering*, vol.60, no.5, pp.1414-1421, May 2013
9. F. J. Lane, M. Huyck, P.R. Troyk, K. Schug; "Responses of potential users to the intracortical visual prosthesis: final themes from the analysis of focus group data" *Disability and Rehabilitation: Assistive Technology*, Vol. 7, No. 4 , Pages 304-313, July 2012
10. H. Zhe, P. Troyk, G. DeMichele, K. Kayvani, S. Suh, "Intrinsic Activation of Iridium Electrodes over a Wireless Link" 34th Annual International Conference of the IEEE EMBS pp. 2788-2791, 2012
11. G.Kaskhedikar, P.R. Troyk, "Identifying the challenges in the development of an effective intracortical visual prosthesis system: Utilization of patient feedback" *Proceedings 7th World Congress on Visual Prostheses: Eye and the Chip* 2012 (Poster presentation)
12. Philip R. Troyk, Sungjae Suh, Zhe Hu, Kevin Kayvani, Glenn DeMichele, and Douglas Kerns, "Assessment Of Technology For An Intracortical Visual Prosthesis" *ARVO Meeting Abstracts March 26, 2012* 53:5552, 2012
13. Frank J. Lane, Margaret H. Huyck, and Philip R. Troyk, "The Experiences Of Recipients Of A Cortical Visual Prosthesis: A Preliminary Analysis Of Nine Participants Expressed Motivation, Decision-making Process, Risks, And Functional Use Of Phosphenes," *ARVO Meeting Abstracts March 26, 2012* 53:5553, 2012
14. Margaret H. Huyck, Frank Lane, Kenneth Schug, and Philip Troyk, "Looking Forward by Looking Back: Comparing Anticipations with Actual Experiences with a Visual Cortical Implant Prosthesis," *ARVO Meeting Abstracts March 26, 2012* 53:5554, 2012

Presentations during the post-award notification/pre-award start date period

15. P. Troyk, F. Lane, 17th Annual Conference of the International Functional Electrical Stimulation Society, Banff, Alberta, CA, "Experiences of Recipients of Cortical Visual Prosthesis Implants - Lessons for all Neural Prostheses," September 12, 2012 (invited presentation)
16. F. Lane, P. Troyk, "Intracortical Visual Prosthesis: Assessing Readiness for a Clinical Trial," 7th World Congress on Visual Prostheses, Detroit MI, September 11, 2012. (invited presentation)
17. Philip R. Troyk, "Intracortical Visual Prosthesis – Assessing Readiness for a Clinical Trial" *Proceedings 7th World Congress on Visual Prostheses, Congress on Visual Prostheses: Eye and the Chip, Detroit MI, September 12, 2013*
18. Philip R Troyk "Intracortical Visual Prosthesis: Status of the Clinical Trial Preparations" *Proceedings 8th World Congress on Visual Prostheses, Congress on Visual Prostheses: Eye and the Chip, Detroit MI, September 28 - 30, 2014*
19. F. Lane "Analysis and results of interviews of fourteen recipients of a cortical vision implant," *Proceedings 8th World Congress on Visual Prostheses, Congress on Visual Prostheses: Eye and the Chip, Detroit MI, September 28 - 30, 2014*

CONCLUSION

Progress towards the clinical trial deployment of the ICVP made possible through the work performed under this project has been good. Examination of the accomplishments, as detailed above, demonstrate that essential steps have been made towards the goal of this project: preparation for the clinical trial.

During the past year, the slow start of the work in year one has been compensated for. In the final year 3, made possible by the TATRC-approved one-year no cost extension, it is anticipated that all the goals of the project will be achieved.

We feel that for accomplishing the ultimate goal of the project: submission of an IDE to the FDA, the no-cost extension will allow for this accomplishment by the end of the grant period.